

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in this application:

Claim 1 (cancelled)

Claim 2 (currently amended) The cellular expression system of claim 11 4, wherein the rec element is included in the first integration cassette.

Claim 3 (currently amended) The cellular expression system of claim 11 4, wherein the rec element is included in the first target cassette.

Claim 4 (currently amended) The cellular expression system of claim 11 4, wherein the recombinase activity is selected from the group consisting of Flp recombinase, Cre recombinase, Int recombinase, Sin recombinase and Hin recombinase.

Claim 5 (currently amended) The cellular expression system of claim 11 4, wherein the host cell is selected from the group consisting of mammalian cells, yeast cells and bacterial cells.

Claim 6 (currently amended) The cellular expression system of claim 11 4, wherein the first integration cassette further comprises a polycistronic element.

Claim 7 (currently amended) The cellular expression system of claim 11 4, wherein the first integration cassette further comprises a tag TAG-sequence.

Claim 8 (currently amended) The cellular expression system of claim 11 4, wherein the first target element further comprises a first target gene and a first selectable marker gene.

Claim 9 (previously presented) The cellular expression system of claim 8, wherein the first target cassette further comprises a polycistronic element.

Claim 10 (currently amended) The cellular expression system of claim 11 4, wherein the first target cassette further comprises a tag TAG-sequence.

Claim 11 (currently amended) A ~~The~~ cellular expression system ~~of claim 1 further~~ comprising:

- a. a first integration cassette comprising
 - i. a first promoter operably linked to
 - ii. a first exchangeable reporter segment comprising a first scorable
homeostatic reporter element, which comprises at least one scorable reporter
gene, the first scorable homeostatic reporter element linked at its 5' end to a first
recombinase recognition site, and at its 3' end to a second recombinase
recognition site;

wherein the first integration cassette is capable of stable and random insertion into a first discrete genomic position in a host cell, thereby creating a recombinant cell population;

b. a first target cassette comprising a first exchangeable target segment comprising:

i. a third recombinase recognition site, capable of recognizing the first recombinase recognition site in the first integration cassette;

ii. a first target element; and

iii. a fourth recombinase recognition site, capable of recognizing the second recombinase recognition site in the first integration cassette;

wherein the first target element is linked at its 5' end to the third recombinase recognition site, and at its 3' end to the fourth recombinase recognition site; and

c. at least one rec element encoding at least one recombinase activity recognizing the recombinase recognition sites of a and b,

wherein introduction of the rec element and the first target cassette to the recombinant cell population results in site-specific substitution of the first exchangeable reporter segment with the first exchangeable target segment at the first discrete genomic position;

d. a second integration cassette ~~which comprises~~ comprising

i. a second promoter operably linked to

ii. a second exchangeable reporter segment ~~having~~ comprising a second scorable homeostatic reporter element, which comprises at least one scorable reporter gene and an exchangeable reporter gene, the second scorable homeostatic

reporter element linked at its 5' end to a fifth recombinase recognition site, and at its 3' end to a sixth recombinase recognition site;

wherein the second integration cassette is capable of stable and random insertion into ~~a one or more~~ second discrete genomic position in ~~a mammalian~~ the host cell; and

e. a second target cassette comprising a second exchangeable target segment having comprising:

i. a seventh recombinase recognition site, capable of recognizing the fifth recombinase recognition site in the second integration cassette;

ii. a second target element; and

iii. an eighth recombinase recognition site, capable of recognizing the sixth recombinase recognition site in the second integration cassette;

wherein the second target element is linked at its 5' end to the seventh recombinase recognition site, and at its 3' end to the eighth recombinase recognition site; and

f. a recombinase activity capable of recognizing the recombinase recognition sites of d and e;

wherein introduction of the second target cassette to the recombinant cell population results in site-specific substitution of the second exchangeable reporter segment with the second exchangeable target segment at the second discrete genomic position.

Claim 12 (currently amended) The cellular expression system of claim 11, wherein the second integration cassette further comprises a tag ~~TAG~~ sequence.

Claim 13 (previously presented) The cellular expression system of claim 11, wherein the second integration cassette further comprises a polycistronic element.

Claim 14 (previously presented) The cellular expression system of claim 11, wherein the second target element further comprises a second target gene and a selectable marker.

Claim 15 (previously presented) The cellular expression system of claim 14, wherein the second target cassette further comprises a polycistronic element.

Claim 16 (currently amended) The cellular expression system of claim 11, wherein the second target cassette further comprises a tag TAG-sequence.

Claim 17 (previously presented) The cellular expression system of claim 11, wherein the first and second target elements each encode one subunit of a protein complex.

Claim 18 (previously presented) The cellular expression system of claim 17, wherein the protein complex is an antibody.

Claim 19 (previously presented) The cellular expression system of claim 11, wherein the first and second target elements encode one or more cloning sites.

Claim 20 (withdrawn) An antibody library comprising:

a cell population, each cell of the cell population having a first integration cassette and a second integration cassette stably integrated at discrete genomic positions;

the first integration cassette comprising a promoter operably linked to a first nucleic acid encoding a first peptide for an antibody, the first nucleic acid linked at its 5' end to a first recombinase recognition site, and at its 3' end to a second recombinase recognition site; and

the second integration cassette comprising a promoter operably linked to a second nucleic acid encoding a second peptide for an antibody, the second nucleic acid linked at its 5' end to a third recombinase recognition site and at its 3' end to a fourth recombinase recognition site;

whereby the first and second nucleic acids are expressed at equal levels in each cell of the cell population.

Claim 21 (withdrawn) The antibody library of claim 20, wherein the first nucleic acid comprises variable sequences.

Claim 22 (withdrawn) The antibody library of claim 20, wherein the second nucleic acid comprises variable sequences.

Claim 23 (withdrawn) The antibody library of claim 20, wherein the first peptide is an antibody light chain peptide and the second peptide is an antibody heavy chain peptide.

Claim 24 (withdrawn) The antibody library of claim 20, wherein the first and second peptides are Fab peptides.

Claim 25 (withdrawn) The antibody library of claim 20, wherein the first and second peptides are Fab' peptides.

Claim 26 (withdrawn) The antibody library of claim 20, wherein the first and second nucleic acids encode a humanized antibody peptide.

Claims 27-29 (cancelled)

Claim 30 (withdrawn) A method for selecting a transformed cell population ~~capable of exchanging nucleic acid segments~~, comprising:

- a. obtaining a first integration cassette as in claim 11(a) ~~1(a)~~;
- b. introducing the first integration cassette into cells, creating a recombinant cell population with the first integration cassette stably inserted at a ~~one or more~~ first discrete genomic positions within each cell;
- c. scoring the level of expression of the first scorable homeostatic reporter element; and
- d. selecting from the recombinant cell population those cells scoring a first predetermined level of expression for the first scorable homeostatic reporter element.

Claim 31 (withdrawn) The method of claim 30, further comprising:

- e. introducing to the selected recombinant cell population
 - i. a first target cassette as in claim 11(b) ~~1(b)~~; and
 - ii. a rec element encoding recombinase activity recognizing the recombinase recognition sites of the first integration cassette and the first target cassette;

whereby the first exchangeable target segment is substituted for the first exchangeable reporter segment at the first discrete genomic positions.

Claim 32 (withdrawn) The method of claim 31, wherein the recombinase activity of step (e) is chosen from the group consisting of Flp recombinase, Cre recombinase, Int recombinase, Sin recombinase and Hin recombinase.

Claim 33 (withdrawn) The method of claim 30, wherein the first discrete genomic positions of step (b) are chromosomal.

Claim 34 (withdrawn) The method of claim 30, wherein the first discrete genomic positions of step (b) are extrachromosomal.

Claim 35 (withdrawn) The method of claim 30, wherein the scorable reporter gene encodes a surface antigen.

Claim 36 (withdrawn) The method of claim 31, wherein the first target element further comprises a first target gene and a first selectable marker gene.

Claim 37 (withdrawn) The method of claim 36, wherein substitution of the first exchangeable target segment for the first exchangeable reporter segment is monitored by screening for the absence of the scorable reporter gene and the presence of the first selectable marker gene.

Claim 38 (withdrawn) The method of claim 30, wherein step (d) further comprises isolating a single cell from the population of cells scoring a first predetermined level of expression for the first scorable homeostatic reporter element, and

the method further comprising:

e. expanding the single cell to form a clonal cell population, wherein the first integration cassette is stably inserted at the same first discrete genomic positions within each cell of the clonal cell population.

Claim 39 (withdrawn) The method of claim 31, wherein the first target element of step (e) has a secretory signal element.

Claim 40 (withdrawn) The method of claim 31, further comprising:

f. obtaining a second integration cassette as in claim 11(d);

- g. introducing the second integration cassette into the recombinant cell population of claim 30, thereby creating a second recombinant cell population with the second integration cassette inserted randomly at one or more second discrete genomic positions within each cell of the second recombinant cell population;
- h. scoring the level of expression of the second scorable homeostatic reporter element for each cell of the second recombinant cell population; and
- i. selecting from the second recombinant cell population those cells scoring a second predetermined level of expression for the second scorable homeostatic reporter element;

wherein the selected cells comprise the second integration cassette stably integrated at one or more second discrete genomic positions and the first integration cassette stably inserted at one or more first discrete genomic positions within each cell.

Claim 41 (withdrawn) The method of claim 40, wherein the first scorable homeostatic reporter element and the second scorable homeostatic reporter element are expressed at equivalent levels.

Claim 42 (withdrawn) The method of claim 40, wherein the first scorable homeostatic reporter element and the second scorable homeostatic reporter element are expressed at a preselected ratio.

Claim 43 (withdrawn) The method of claim 40, wherein the second integration cassette further comprises a polycistronic element.

Claim 44 (withdrawn) The method of claim 40, wherein the second integration cassette further comprises a tag TAG sequence.

Claim 45 (withdrawn) The method of claim 40, wherein the second scorable homeostatic reporter element comprises a scorable reporter gene and an exchangeable reporter gene that differs from the first scorable homeostatic reporter element.

Claim 46 (withdrawn) The method of claim 40, further comprising:
introducing to the second recombinant cell population;

- i. a first target cassette as in claim 11(b) ~~1(b)~~;
- ii. a second target cassette as in claim 11(c);
- iii. a rec element encoding recombinase activity recognizing the recombinase recognition sites of the first and second integration cassettes and first and second target cassettes;

wherein the first exchangeable target segment is substituted for the first exchangeable reporter segment at the first discrete genomic positions, and the second exchangeable target segment is substituted for the second exchangeable reporter segment at the second discrete genomic positions.

Claim 47 (withdrawn) The method of claim 46, wherein the first target cassette and the second target cassette encode subunits of a multi-subunit complex.

Claim 48 (withdrawn) The method of claim 47, wherein the multi-subunit complex is an enzyme.

Claim 49 (withdrawn) The method of claim 47, wherein the multi-subunit complex is an antibody.

Claim 50 (withdrawn) A site-specific expression system comprising a recombinant cell population having an integration cassette as in claim 11(a) ~~1(a)~~, wherein the integration cassette is stably and randomly inserted at one or more discrete genomic positions within each cell of the recombinant cell population and wherein the homeostatic reporter element and the target element is expressed.

Claim 51 (withdrawn) An antibody producing recombinant cell population, each cell of the recombinant cell population having a first integration cassette as in claim 11(a) ~~1(a)~~ and a second integration cassette as in claim 11(e), wherein each integration cassette is stably and randomly inserted at a first and second discrete genomic position, respectively, in each cell of the recombinant cell population, and wherein the first and second integration cassette is substituted with a first exchangeable target segment as in claim 11(b) ~~1(b)~~ and a second exchangeable target segment as in claim 11(f), wherein the first and second exchangeable target segment encodes an antibody chain, whereby the antibody chains encoded by the first and second exchangeable target segment is expressed at equivalent levels in each cell of the recombinant cell population.

Claim 52 (withdrawn) The antibody producing recombinant cell population of claim 51, wherein the recombinant cell population is clonal in origin.

Claim 53 (withdrawn) The antibody producing recombinant cell population of claim 51, wherein the antibody chains comprise a light chain and a heavy chain.

Claim 54 (withdrawn) The antibody producing recombinant cell population of claim 53, wherein the heavy chain corresponds to a heavy chain Fab fragment.

Claim 55 (withdrawn) The antibody producing recombinant cell population of claim 53, wherein the heavy chain corresponds to a heavy chain Fab' fragment.

Claim 56 (withdrawn) A recombinant expression cell line comprising: a recombinant cell line having an integration cassette as in claim 11(a) ~~1(a)~~, wherein the integration cassette is stably inserted at a discrete genomic position that is identical in each cell of the recombinant cell line.

Claim 57 (withdrawn) The recombinant expression cell line of claim 56, wherein the integration cassette further comprises a polycistronic element.

Claim 58 (withdrawn) The recombinant expression cell line of claim 56, wherein the integration cassette further comprises a tag ~~TAG~~ sequence.

Claim 59 (withdrawn) A method of making an antibody library comprising:

- a. obtaining a second recombinant cell population as in claim 40(g);
wherein the first scorable homeostatic reporter element and the second scorable homeostatic reporter element are expressed at equivalent levels in the second recombinant cell population;
- b. introducing a first target cassette having a first target element as in claim 11(b) ~~1(b)~~, wherein the first target element encodes a first peptide for an antibody; and
- c. introducing a second target cassette having a second target element as in claim 11(e), wherein the second target element encodes a second peptide for an antibody; whereby the first and second target elements are expressed at equal levels in each cell of the cell population.

Claim 60 (withdrawn) The method of claim 59, wherein the first peptide comprises variable sequences.

Claim 61 (withdrawn) The method of claim 59, wherein the second peptide comprises variable sequences.

Claim 62 (withdrawn) The method of claim 59, wherein the first peptide is an antibody light chain peptide and the second peptide is an antibody heavy chain peptide.

Claim 63 (withdrawn) The method of claim 59, wherein the first and second peptides are Fab peptides.

Claim 64 (withdrawn) The method of claim 59, wherein the first and second peptides are Fab' peptides.

Claim 65 (withdrawn) The method of claim 59, wherein the first and second peptides are humanized antibody peptides.